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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/789,526	02/26/2004	Kenneth W. Dobie	BIOL0002US	9932

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EXAMINER

EPPS FORD, JANET L

ART UNIT	PAPER NUMBER
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1633

MAIL DATE	DELIVERY MODE
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07/24/2008

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/789,526	Applicant(s) DOBIE ET AL.	
	Examiner Janet L. Epps-Ford	Art Unit 1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 09 April 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,4-7,9,13,20-23,46,47,50,52-62 and 66-73 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,4-7,9,13,20-23,46,47,50,52-62 and 66-73 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Claims 1, 4-7, 9, 13, 20-23, 46-47, 50, 52-62, and 66-73 are pending for examination.
2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Response to Arguments

Claim Rejections - 35 USC § 112

3. The rejection of Claims 4-7, 9, 20-23, 46-47, 60, and 68-69 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, is withdrawn in response to Applicant's amendment.
4. The previous indication that claims 1, 13, 50, 52-59, 61-62, and 66-67 are allowable is withdrawn in response to an updated search and the following rejection set forth below.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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6. Claims 1, 4-7, 9, 13, 20-23, 46-47, 50, 52-62, and 66-73 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shoshan et al. (WO0210449) in view of Bennett et al. US Patent No. 6172216, and Wengel et al.

Shoshan et al. describe the following oligonucleotide sequence (SEQ ID NO: 28264): gctgcaagaattgctcatgaatggacccagggaatggaaagaatgccctgattatgtctctgctgg (65 base pairs).

This oligonucleotide is disclosed as an RNA transcript or splice variant of a transcript (see ¶ [0115]).

Shoshan et al. teach that these RNA transcripts can be used as the basis for designing antisense RNA and siRNA. (see ¶ [0111] through [0113]). Exemplary siRNAs according to Shoshan et al. could have up to 29 bp, 25, 22, 21, 20, 15, or 10 base pairs.

SEQ ID NO: 19 of the instant invention is 100% complementary to this sequence.

However, Shoshan et al. does not describe an antisense oligonucleotide or 12 to 50 nucleotides in length targeting the disclosed sequence having the sequence of SEQ ID NO: 19 are recited in the instant claims, or wherein the antisense oligonucleotide comprises the various modifications recited in the instant claims, or pharmaceutical compositions comprising the antisense compounds of the instant invention.

Bennett et al. teach that the incorporation of modified nucleobases into oligomeric compounds, including 5-methylcytosine modifications, is well known in the art for the purpose of increasing the binding affinity of the oligomeric compounds of the invention. (col. 9, lines 5-7). Bennett et al. also discloses wherein the oligonucleotide is

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a 20 base pairs in length, a chimeric oligonucleotide, and comprising 2'-MOE modifications (other positions comprise 2'-deoxy modifications), all 2'-MOE cytosines are 5-methylcytosines, and all linkages are phosphorothioate linkages. Bennett et al. also teach oligomeric compounds of comprising sodium salts, see for example, col. 11, lines 14-23. Additionally, Bennett et al. teach the pharmaceutical compositions and/or formulations comprising the oligonucleotides of the present invention may also include penetration enhancers in order to enhance the alimentary delivery of the oligonucleotides. The penetration enhancers of Bennett et al. include for example, oleic acid, lauric acid, capric acid, myristic acid, palmitic acid, stearic acid, linoleic acid, linolenic acid, and dicaprates see col. 13, lines 10-25).

Additionally, Bennett et al. includes compositions comprising the disclosed oligomeric compounds in combination with a carrier or diluent, see col. 14. The modified therapeutic oligonucleotides of Bennett et al. are disclosed as having increased nuclease stability and increased cellular uptake.

Wengel et al. teach the modification of oligonucleotides to comprise locked nucleosides comprising a bridge between the 2'-O and the 4' carbon atom. Oligonucleotides comprising this modification are described as forming duplexes with higher specificity with its target, and having increased thermostability with its target in comparison to un-modified oligonucleotides.

It would have been obvious to the ordinary skilled artisan to modify the teachings of Shoshan et al. with the teachings of Bennett et al. and Wengel et al. in the design of the instant invention. One of ordinary skill in the art would have been motivated to

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make this modification since, although Shoshan et al. discloses a plurality of oligonucleotide RNA transcripts, the disclosure of this reference clearly suggests designing antisense and siRNA oligonucleotides targeting these sequences. Therefore, although the number of transcripts is numerous, nonetheless the sequences of these oligonucleotide RNA transcripts are disclosed. Moreover, the particular sequence of the oligonucleotide transcript of SEQ ID NO: 28264 is only 65 base pairs. Therefore, since Shoshan et al. explicitly suggests that the ordinary skilled artisan make antisense and siRNA targeting the disclosed sequences, and the prior art teaches how to design antisense and siRNA, there would have been a reasonable expectation of success for the ordinary skilled artisan to design antisense and siRNA targeting the oligonucleotide RNA transcripts of Shoshan et al. Moreover, due to the small number of nucleotides set forth in SEQ ID NO: 28264, and the fact that Bennett et al. teach that antisense oligonucleotides are preferably 20 base pairs in length, the sequence of SEQ ID NO: 19 of the instant invention could be immediately envisioned due to the limited number of possible 20 base pair non-overlapping antisense oligonucleotides that could be designed based upon a sequence of only 65 base pairs.

Furthermore, it would have been obvious to design antisense oligonucleotides comprising the various modifications recited in the instant claims, particularly wherein the claimed oligonucleotide comprising a chimeric structure including a stretch of deoxynucleotides flanked by 2'-O-methoxyethyl modifications, phosphorothioate internucleoside linkages, and 5-methylcytosines, since Bennett et al. clearly teach that oligonucleotides comprising this structure al. are disclosed as having increased

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nuclease stability and increased cellular uptake. Moreover, it would have been obvious to design compounds comprising locked nucleosides comprising a bridge between the 2'-O and the 4' carbon atom. Oligonucleotides comprising this modification are described as forming duplexes with higher specificity with its target, and having increased thermostability with its target in comparison to un-modified oligonucleotides.

Regarding the rationale for combining prior art elements according to known methods to yield predictable results, all of the claimed elements were known in the prior art and one skilled in the art could have combined the element as claimed by known methods with no change in their respective functions, and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Epps-Ford whose telephone number is 571-272-0757. The examiner can normally be reached on M-F, 10:00 AM through 6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Janet L. Epps-Ford/
Primary Examiner, Art Unit 1633

/J. L. E./
Primary Examiner, Art Unit 1633